As Venezuela's public health system collapses, mosquito-borne viruses re-emerge

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Psorophora ferox female, a potential vector for Madariaga virus. Photo taken on Heritage Island, Anacostia River, in Washington, D.C., June 30, 2012. Credit: Wikimedia Commons, CC BY

The ability to predict which virus will cause the next epidemic is a science, an art and a gamble. We have learned through our work in Venezuela that it's always a good idea to pay attention to the cryptic viruses.

During our work on the Zika virus epidemic in Venezuela, we may have spotted the emergence of a potentially dangerous virus that appears to be crossing from horses to humans: Madariaga virus. By using a diverse toolkit of approaches, we were able to look behind the curtains of the Zika virus epidemic to see what might be coming next. Time will tell if Madariaga virus will spread across Venezuela's borders, but continued research will allow us to be prepared if it does.

As scientists, we aim to learn from past outbreaks and hope those lessons are applicable to future situations. We try to be proactive, because being caught unprepared and having to react to an outbreak comes at a cost that is often paid in human lives.

Being prepared includes keeping a close watch on human and animal viruses in circulation. This is referred to as virus surveillance. We pay attention to animal viruses because many of today's deadly viruses such as Ebola virus and Middle East respiratory syndrome coronavirus (MERS-CoV) are animal viruses that now affect humans. Surveillance is especially important for mosquito-transmitted viruses, particularly when public health systems are overburdened and mosquito control is limited.

Moreover, viruses frequently mutate, and it is important to track whether they are changing into more virulent versions. Billions of dollars and countless hours in the laboratory have been invested toward developing vaccines to protect humans and other animals such as horses and livestock against mosquito-transmitted viruses, but vaccines are not available for many of the important viruses.

We began working on mosquito-transmitted viruses during the 2016 outbreak of Zika virus in Venezuela, along with Dr. J. Glenn Morris of the Emerging Pathogens Institute and with Dr. Alberto Paniz-Mondolfi, a physician based in Barquisimeto, Venezuela. We teamed up with the Incubadora Venezolana de la Ciencia, a group of Venezuelan medical students, interns and physicians based in Barquisimeto.

As a native Venezuelan, G. Blohm had watched the country's public health system collapse under the weight of an unprecedented economic crisis. She had watched hundreds of people leave the country. She, too, had left the country with a heavy heart after her family suffered repeated assaults and threats of kidnapping. She had seen better days in this beautiful place and has not stopped believing in the potential of its land and of its people. She knew that Venezuela's crisis could affect neighboring countries and hoped to assist in monitoring the spread of mosquito-transmitted diseases within and across Venezuela's borders.

Because the study of mosquito-transmitted diseases involves an element of chance, we could not have predicted what we would find.

Viruses are often puzzling

Mosquito-transmitted viruses can be deceiving. The illnesses they cause are often misdiagnosed or the virus is not detected. They can hide behind similar early clinical symptoms, yet there can be vast differences in long-term consequences to the patient.

This is true for dengue, Chikungunya, Zika and other mosquito-transmitted viruses, which can elicit similar symptoms during the early phase of infection in those affected, yet the long-term effects can vary significantly. It is therefore important to have the capacity to detect and identify these viruses in diagnostic laboratories.

In preparing for outbreaks of mosquito-transmitted viruses, it's important also to understand the biology of each virus, its genetic makeup, proper methods for diagnosis and the clinical symptoms it can cause.

The genetic code of a virus contains information about its geographic origins and its relatedness to other viruses. Knowing its relatedness to other viruses can sometimes – but not always – give clinicians some clues about the symptoms it may cause. Uncovering the genetic code of a virus requires detection and isolation of the virus in the laboratory.

How to detect a virus

There are several ways to detect a virus: One can look for antibodies in the patient, or if the laboratory has the capacity and the timing is just right, one can actually retrieve (i.e., isolate) the virus from the patient. Some laboratory tests rely on antibodies to discern whether a patient has been infected with a particular virus in the past.

These tests, although common, are less precise and can be misleading: Antibodies to closely related viruses react against similar viruses. This cross-reactivity can confound diagnosis in countries wherein many of the viruses co-exist.

Isolation of a virus is more precise, and it is as much a science as it is an art. The patient's specimen needs to be collected properly, during the right time of infection, and the procedures used need to be just right for each type of virus. Ascertaining the correct procedures for isolating viruses requires years of training and experience. And the processes used require special equipment, instruments and facilities, making them impractical or impossible in resource-strapped laboratories.

Viruses do not cause epidemics in a vacuum. In many cases, there are

social and environmental conditions that set the stage for an outbreak. In Venezuela, the deterioration of the political and economic infrastructure, and the destruction of the country's public health system have created conditions that make the inhabitants of this once prosperous country susceptible to outbreaks. Venezuela, which in the 1950s was the world's fourth wealthiest nation per capita, currently has the highest inflation rate in the world.

Mosquito-transmitted diseases that were once under control such as Dengue Fever have reached record high levels, with no signs of receding. Other less well-known viruses are on the rise in Venezuela: some are inching their way across the barrier between domestic animals and humans. Madariaga virus (MADV) is one such virus which we suspect has crossed this barrier.

Madariaga virus

Madariaga virus is a South American virus that is genetically similar to Eastern equine encephalitis virus (EEEV). Scientists know much more about EEEV, which is a mosquito-transmitted virus that infects horses, humans and other animals. Although rare in humans, EEEV causes severe infections wherein up to 33 percent of those infected die, usually due to encephalitis, or inflammation of the brain. Those that survive have significant brain damage. There is no vaccine to protect humans against EEEV or cure for the illnesses it causes.

Recent genetic studies reveal that MADV is distinct from but nevertheless closely related to EEEV, and is found in Central and South America. Antibody tests suggest the virus infects humans and caused an outbreak among Panamanians in 2010, but until now, the virus itself only had been isolated from or detected in horses, rodents and mosquitos.

During our work on the Zika outbreak in Venezuela, we may have

unveiled a more cryptic outbreak of MADV in humans. We detected the virus in the blood of a Venezuelan child who had initially been thought to have Zika. The child had developed a fever, rash and joint pains, but his infection did not progress. And, he did not develop encephalitis. The child developed an infection at a time when veterinarians reported cases of neurologic disease among horses in the locality of the patient's area of residence; the horses were thought to be infected with EEEV. Whereas laboratory confirmation of EEEV or MADV was not possible due to the situation in Venezuela, it is plausible that the horses were infected with MADV. The presence of the virus in this child, though, provides evidence that MADV infects humans.

We scientists have learned repeatedly that viruses like MADV and their mosquito vectors do not honor national borders, and that preventing their spread into surrounding areas requires international efforts. Preparedness and continued research will allow us to come out ahead of the next epidemic, which may very well have its origins in a country whose public health infrastructure is in disrepair. The entire global community needs continued research on the biology, the genetics and the clinical symptoms of MADV.

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